

## Gender differences and hospitalization for COPD: an analysis of data from Puglia (Italy)

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**Summary. Background.** The prevalence and mortality rate of chronic obstructive pulmonary disease (COPD) in women have more than doubled over the past 20 years in industrialized countries while remaining unchanged in men. International guidelines for the diagnosis and treatment of COPD make gender-neutral recommendations. However, appreciation and knowledge of gender differences may improve management and treatment of this disease. Yet, limited data exist in this regard. **Objectives.** The aim of this study was to carefully evaluate frequency and characteristics of hospitalizations among COPD patients in Puglia (Italy) in the years from 2001 to 2011, with an emphasis on gender differences. **Methods.** Data from the Archive of the Regional Hospital Discharge Forms for the 2001-2011 period were used for this analysis. The codification of clinical information of diagnoses and procedures performed during the hospital stay is ICD-9, version 2007. **Results.** The annual number of hospitalizations among COPD patients decreased from 13,398 in 2001 to 6,963 in 2011, equivalent to a 48% reduction in the 11-year observation period. However, the percentage of hospitalizations among females increased from 27.8% in 2001 to 35.6% in 2011. Reporting of spirometry or arterial blood gas analysis data at discharge was higher in males than in females during the observation period. **Conclusions.** This study shows that, despite an overall reduction in the number of hospitalizations among patients with COPD between 2001 and 2011 in Puglia (Italy), the percentage of female patients hospitalized increased significantly. If validated, this finding may have significant therapeutic and prognostic implications

**Key words:** COPD, gender differences, hospitalization.

### *Differenze di genere e ospedalizzazione nella BPCO: una analisi dei dati della Puglia*

**Riassunto. Background.** La prevalenza e la mortalità per broncopneumopatia cronica ostruttiva (BPCO) nel sesso femminile sono più che raddoppiate negli ultimi 20 anni nei paesi industrializzati, mentre negli uomini sono rimaste invariate. Le linee guida internazionali per la diagnosi e il trattamento della BPCO formulano raccomandazioni indifferenti rispetto al genere. Tuttavia la considerazione e la conoscenza delle differenze di genere potrebbe migliorare la gestione e il trattamento della malattia. Esistono però dati limitati sull'argomento. **Obiettivi.** Lo scopo di questo studio è stato di valutare attentamente la frequenza e le caratteristiche delle ospedalizzazioni tra le pazienti e i pazienti con BPCO in Puglia tra il 2001 e il 2011, evidenziando le differenze di genere. **Metodi.** Per l'analisi sono stati utilizzati

i dati dell'Archivio Regionale delle dimissioni ospedaliere nel periodo 2001-2011. La codifica dell'informazione clinica delle diagnosi e delle procedure eseguita durante i ricoveri ospedalieri è quella dell'ICD-9, versione 2007. **Risultati.** Il numero annuale di ospedalizzazioni dei soggetti con BPCO si è ridotto da 13.398 nel 2001 a 6963 nel 2011 (48% nel corso degli 11 anni del periodo di osservazione). Tuttavia, la percentuale di ospedalizzazioni di pazienti di sesso femminile è passata dal 27,8% nel 2001 al 35,6% nel 2011. Durante il periodo di osservazione, alla dimissione, si evidenziava una più frequente esecuzione di spirometria ed emogasanalisi arteriosa nei pazienti di sesso maschile. **Conclusioni.** Questo studio evidenzia che, nonostante una riduzione generale del numero delle ospedalizzazioni tra i soggetti con BPCO tra il 2001 e il 2011 in Puglia, la percentuale delle pazienti ospedalizzate è aumentata in modo significativo. Se tale dato sarà confermato, potrebbe avere significative implicazioni terapeutiche e prognostiche.

**Parole chiave:** BPCO, differenze di genere, ospedalizzazione.

### Introduction

Chronic obstructive pulmonary disease (COPD) is currently the fourth leading cause of death in the developed world. According to data from the World Health Organization, COPD will become the world's third leading cause of death in 2030, whereas in 2020 COPD-related disability will rise from ninth to fifth place in terms of Disability-Adjusted Life Years (DALYs)<sup>1</sup>. Currently, the prevalence of COPD in the general population is estimated to stand at 5-15% with a substantial cost in social and economic terms<sup>2</sup>. The economic impact of COPD, which is a function of disease severity, is mainly driven by emergency room visits and hospital admissions<sup>3</sup>.

Chronic respiratory diseases are among the most interesting areas of investigation with regard to gender differences because of evidence of growing "feminization" of several diseases that previously documented a male preponderance<sup>4-5</sup>. COPD, the prototype of a chronic respiratory disease, has been traditionally considered almost exclusively a 'man's disease'<sup>6</sup>. However, a seminal study published in 2000 and carried out in the UK between 1990 and 1997, showed a 69% increase in the prevalence of COPD among women compared to 25% among men<sup>5</sup>. The prevalence and mortality rates

of COPD in women have more than doubled over the past 20 years in industrialized countries while remaining essentially unchanged in men<sup>7-8</sup>. Furthermore, over the past two decades, in the US and in Europe, COPD-related mortality rates have grown faster in women<sup>7-8</sup>.

An understanding of the causes of these epidemiological changes requires knowledge of the determinants of the disease and their distribution in both sexes. COPD is believed to be the result of a complex interaction between genetic and multiple environmental factors such as cigarette smoke, dust, vapors, fumes and chemicals from occupational exposure, and indoor and outdoor pollution<sup>9</sup>.

Increased prevalence and mortality of COPD among women compared with men is usually attributed to a rise in smoking prevalence in women<sup>10-11</sup>. However, a number of studies have also highlighted the crucial role of occupational and domestic exposure, including some forms that have been traditionally male domains<sup>12-14</sup>. The risk for women's respiratory health in the workplace is mainly due to exposure to detergents (cleaning, catering and restaurants), sterilizing products and disinfectants, pesticides and organic dust (agriculture, food production), chemical products and solvents (textiles and clothing) and to bad air quality and second-hand tobacco smoke (office work and call centers)<sup>15</sup>.

A greater susceptibility to the toxic effects of cigarette smoking and other pollutants and an increased susceptibility of women to COPD have also been reported<sup>10,16</sup>. Indeed, numerous studies carried out in patients with COPD have shown that, following similar exposure to cigarette smoke, women have a sharper decline in respiratory function (in particular, forced expiratory volume in one second [FEV1]), as well as a more severe stage of the disease, compared to male subjects. The main hypotheses behind the increased susceptibility of women to the harmful effects of smoking include smaller airway caliber, increased bronchial reactivity, and the role of estrogen that can induce the conversion of some cigarette components into their metabolically active form, with consequent lung injury<sup>9,17</sup>.

Moreover, women tend to underestimate symptoms, which, in turn, can lead to increased disease severity, worse quality of life, increased frequency of hospitalizations and higher mortality<sup>7,18-22</sup>.

Finally, COPD-associated co-morbidities, such as cardiovascular disease and depression, are more frequent in women than in men<sup>23-24</sup>. Despite these differences, current guidelines for the diagnosis and treatment of COPD do not make different recommendations for female and male patients.

The aim of this study was to carefully investigate frequency and characteristics of hospitalizations for COPD in Puglia (Italy) between 2001 and 2011, with an emphasis on gender differences.

## Methods

We analyzed the patient discharge database (SDO) from Puglia's hospitals in the period from 2001 to 2011. The codification of clinical information of diagnoses and procedures performed during the hospital stay was ICD-9, version 2007.

The analysis was performed selecting hospital admissions for COPD with and without exacerbation (ICD9 codes 491.20 and 491.21) using ICD9 codes in the "principal diagnosis" field of the database as the search key. We analyzed all admissions made in health-care facilities in Puglia, and calculated mean hospitalization length of stay, average age of hospitalized patients and frequency of comorbidities that can modify the natural history of COPD, such as diabetes (ICD9 code 250.x), obesity (ICD-9 code 278.0), anxiety (ICD9 code 300.x), atrial fibrillation (ICD9 code 427.31), essential hypertension (ICD9 code 401), and heart failure (ICD9 code 428). The mean length of stay was calculated using the ratio of the sum of days spent in hospital, taken from hospital discharge records, and the number of admissions.

For comorbidities, secondary diagnosis fields of the database were examined for 1-5 years.

The analysis of procedures such as spirometry and arterial blood gas analysis (ABG) was carried out using the appropriate codes ICD-9-CM (89.37 and 89.65) and calculating the proportion of SDO that reported these procedures by sex and unit.

The analysis is descriptive and was performed with the quantitative method. The nominal variables are expressed in percentage, whereas continuous variables are expressed either as percentage or average. Proportion were compared using the specific test with Stata MP11 software.

## Results

From 2001 to 2011 there were 127,062 admissions for COPD in Puglia, of which 27,558 (21.68%) were due to disease exacerbation and 99,504 (78.3%) to causes other than exacerbation.

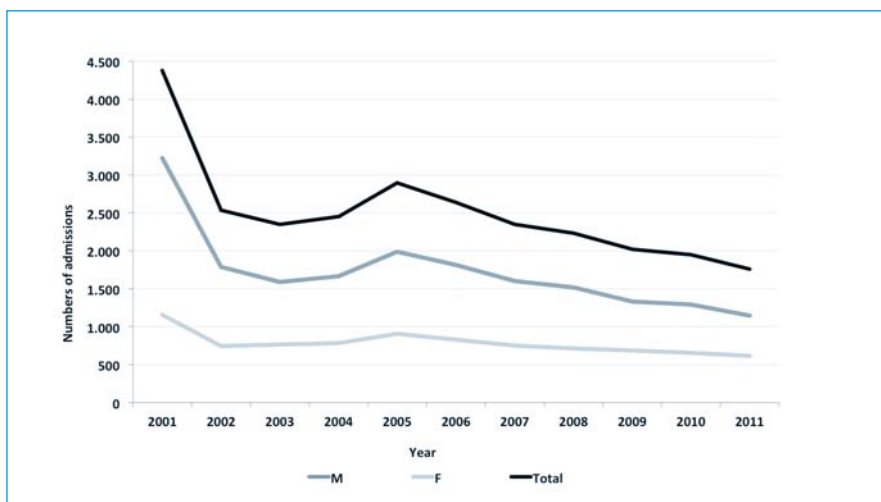
The annual number of hospitalizations for COPD decreased from 13,398 in 2001 to 6,963 in 2011, with a 48% reduction in the 11-year observation period.

In particular, a more substantial reduction occurred in the number of hospitalizations for COPD without exacerbation (e.g., from 32.7% in 2001 to 25.3% in 2011,  $z = 28.3$ ,  $p < 0.05$  - Table 1).

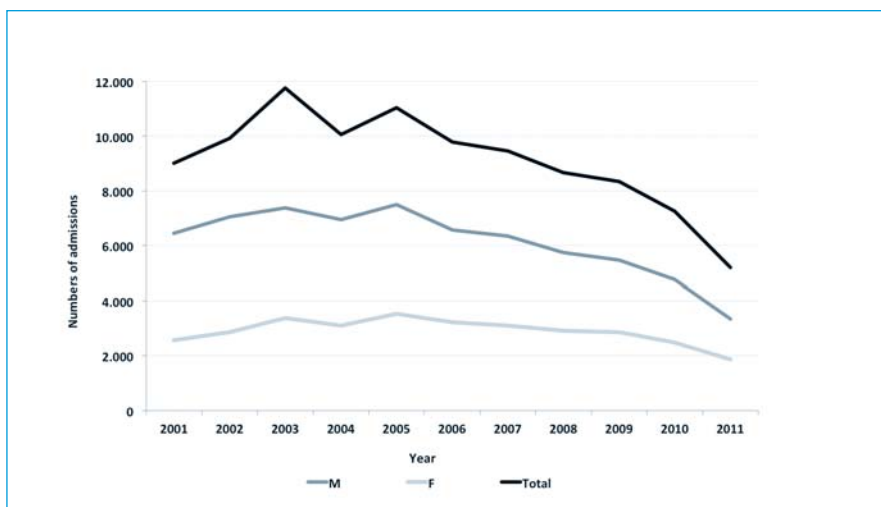
The number of admissions with and without acute exacerbation, both overall and stratified by gender, is shown in Figure 1 and 2, respectively. Gender distribution changed considerably during the 11 years of obser-

**Table 1.** Number of admissions for chronic obstructive pulmonary disease (COPD) and distribution of admissions for COPD with and without exacerbation, per year. Puglia, 2001-2011:

Year	Admissions for COPD without exacerbation		Admissions for COPD with exacerbation		Total admissions	
	N	% (CI 95%)	N	% (CI 95%)	N	%
2001	4,380	32.7 (31.9-33.5)	9,018	67.3 (66.5-68.1)	13,398	100.0
2002	2,537	20.4 (19.7-21.1)	9,921	79.6 (78.9-80.3)	12,458	100.0
2003	2,350	17.9 (17.2-18.6)	10,758	82.1 (81.4-82.6)	13,108	100.0
2004	2,449	19.6 (18.9-20.3)	10,060	80.4 (79.7-81.1)	12,509	100.0
2005	2,897	20.8 (20.1-23.6)	11,035	79.2 (79.5-79.9)	13,932	100.0
2006	2,641	21.2 (20.5-23.6)	9,789	78.8 (78.1-79.5)	12,430	100.0
2007	2,350	19.9 (19.2-20.6)	9,456	80.1 (79.4-80.8)	11,806	100.0
2008	2,231	20.5 (19.7-21.3)	8,662	79.5 (78.7-80.3)	10,893	100.0
2009	2,017	19.5 (18.7-20.3)	8,349	80.5 (79.7-81.3)	10,366	100.0
2010	1,947	21.2 (20.4-22.0)	7,252	78.8 (78.0-79.6)	9,199	100.0
2011	1,759	25.3 (24.3-26.3)	5,204	74.7 (73.7-75.7)	6,963	100.0
<b>Total</b>	<b>27,558</b>	<b>27.7 (27.5-27.9)</b>	<b>99,504</b>	<b>78.3 (78.1-78.5)</b>	<b>127,062</b>	<b>100.0</b>



**Figure 1.** Number of admissions for chronic obstructive pulmonary disease without exacerbation, per year and sex. Puglia, 2001-2011.



**Figure 2.** Number of admissions for chronic obstructive pulmonary disease with exacerbation, per year and sex. Puglia, 2001-2011.

vation; indeed, the M: F ratio decreased from 2.6:1 in 2001 to 1.8:1 in 2011 (Table 2). Conversely, the percentage of hospitalizations of female subjects increased by approximately 8%, i.e. from 27.8% in 2001 to 35.6% in 2011 ( $z = 32.8, p < 0.05$ ). No sex-differences were observed between admissions with and without exacerbation.

On average, female patients were 1 year older than males and the age of hospitalized patients increased by approximately 1 year during the observation period in both sexes (Table 3).

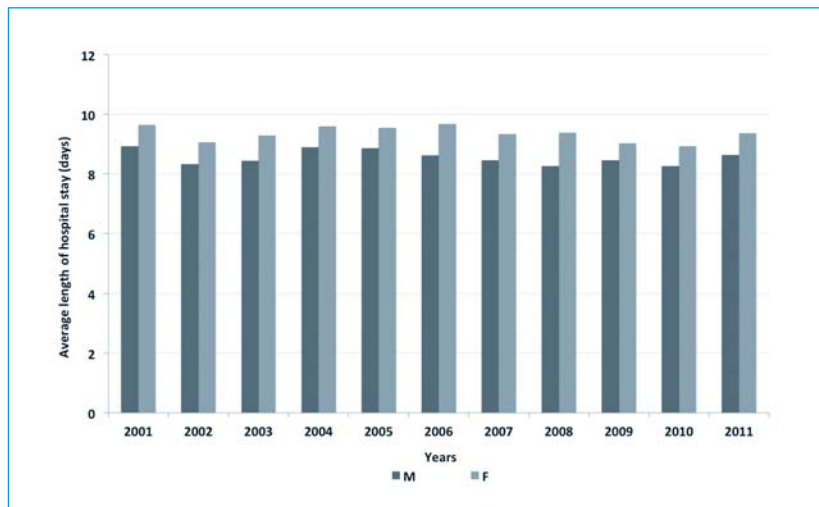
**Table 2.** Male to female ratio of patients hospitalized for chronic obstructive pulmonary disease. Puglia, 2001-2011.

Years	M:F
2001	2.6:1
2002	2.5:1
2003	2.2:1
2004	2.2:1
2005	2.1:1
2006	2.1:1
2007	2.1:1
2008	2.0:1
2009	1.9:1
2010	1.9:1
2011	1.8:1

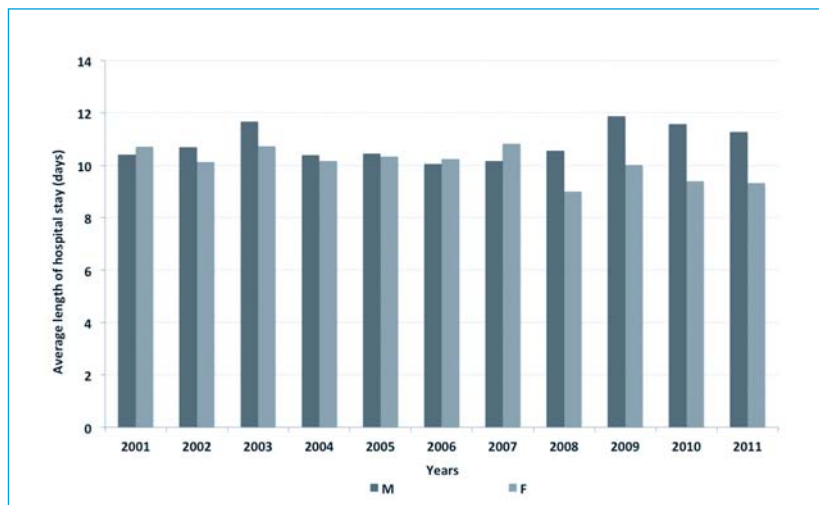
**Table 3.** Average age of patients hospitalized for chronic obstructive pulmonary disease with and without exacerbation, per year and per sex. Puglia, 2001-2011.

Year	Average age M (years)	Average age F (years)
2001	70.7	71.8
2002	71.5	72.8
2003	71.8	73.7
2004	71.9	73.3
2005	72.2	73.8
2006	72.6	73.7
2007	72.8	74.4
2008	72.7	74.3
2009	72.6	73.7
2010	72.9	73.5
2011	72.1	72.9

Between 2001 and 2011, the average length of stay was longer for exacerbation of COPD among female subjects, whereas it was longer among male patients without exacerbation during the last three years of the observation period (Figures 3 and 4). The analysis of the average length of stay stratified by unit shows a reduction of admissions of patients without COPD exacerbation in all units, while among patients admitted due to disease exacerbation the average length of stay remained unchanged, with the exception of rehabilitation units in which the average length of stay was halved.



**Figure 3.** Average length of hospitalization for chronic obstructive pulmonary disease with exacerbation, per year and sex. Puglia, 2001-2011.



**Figure 4.** Average length of hospitalization for chronic obstructive pulmonary disease without exacerbation, per year and sex. Puglia, 2001-2011.

In addition, when we limited our analysis to the last three years of observation (2009-2011), we observed that the percentage of patients readmitted was lower among females both in 2010 and 2011 (Figure 5).

Throughout the observation period, the percentage of SDO reporting spirometry or arterial blood gas analysis was higher among male patients for both procedures (Figures 6 and 7).

Finally, Table 4 summarizes the comorbidities reported in SDO. The prevalence of obesity, diabetes, atrial fibrillation and anxiety disorders was higher among female than male patients. On the other hand, there were no sex-differences for the other comorbidities considered.

## Discussion

Hospitalization estimates are important to quantify the burden of a disease and to assess quality of care, but they are representative of only a portion of patients with COPD because, with increasing frequency, they are treated at home and followed up in outpatient clinics<sup>25</sup>. In fact, the number of admissions decreased significantly during the 11-year observation period, mostly because regional strategies for management of patients with COPD have encouraged home treatment and care, in order to limit hospitalization to severe cases. In Puglia, the reduction in the number of admissions was mainly observed in male subjects, whereas the number of admissions increased among females, which is in line with the European statistics<sup>26-27</sup>.

Although the analysis of SDOs reported the main diagnostic procedures performed during hospitalization, they did not provide information about the results of such procedures. As such, the hospitalization data allow assessing disease severity only through proxies such as average patient age at admission and comorbidities. An analysis of the proxies shows that, in accordance with previous studies<sup>21</sup>, COPD tends to be more severe in women. In fact, female patients hospitalized for COPD in Puglia between 2001 and 2011 were older than men and needed a longer hospital stay.

As for comorbidities, our data are consistent with the relevant literature on this topic with regard to cardiovascular diseases and anxiety disorders, whereas the higher prevalence of diabetes among females hospitalized for COPD represents, to the best of our knowledge, a novel finding<sup>23-24</sup>. The use of diagnostic procedures such as lung function test and blood gas analysis was clearly greater during the hospitalization of male patients throughout the entire observation period, suggesting that a more thorough diagnostic approach is applied to men. In this regard, it has been recently shown that a correct diagnosis is made in 64% of the

male patient population and only in 49% of the female population, probably due to bias with regard to different access to respiratory diagnostics in the two sexes<sup>21</sup>.

Our study has major limitations, the most significant being the data source. While SDOs represent a robust and reliable source of information, they provide data only on patients who have been hospitalized. In addition, they do not report information on the results of investigations performed, thus not allowing to stage patients for disease severity. Furthermore, we limited our analysis to patients who were hospitalized for COPD and account only for a minority of hospital admissions, although it could be argued that COPD is a typical example of chronic illness.

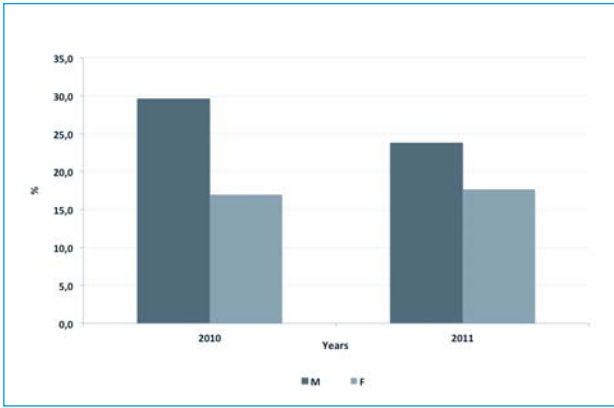
In summary, this study shows that, despite an overall reduction in the number of COPD patients hospitalized between 2001 and 2011 in Puglia (Italy), the percentage of female COPD patients admitted to hospital increased significantly during this period of time. Further studies are needed to clarify the determinants of this phenomenon, which, if validated, may have significant therapeutic and prognostic implications.

### Key messages

- The prevalence and mortality rate of COPD in women have more than doubled over the past 20 years in industrialized countries while remaining unchanged in men.
- Number of admissions decreased significantly during the 11-year observation period (2001-2011) in Puglia (Italy), mostly because regional strategies for management of patients with COPD have encouraged home treatment and care, in order to limit hospitalization to severe cases.
- In Puglia, the reduction in the number of admissions for COPD was mainly observed in male subjects.
- Despite an overall reduction in the number of hospitalizations among patients with COPD between 2001 and 2011 in Puglia (Italy), the percentage of female patients hospitalized increased significantly.
- Reporting of spirometry or arterial blood gas analysis data at discharge was higher in males than in females during the observation period.

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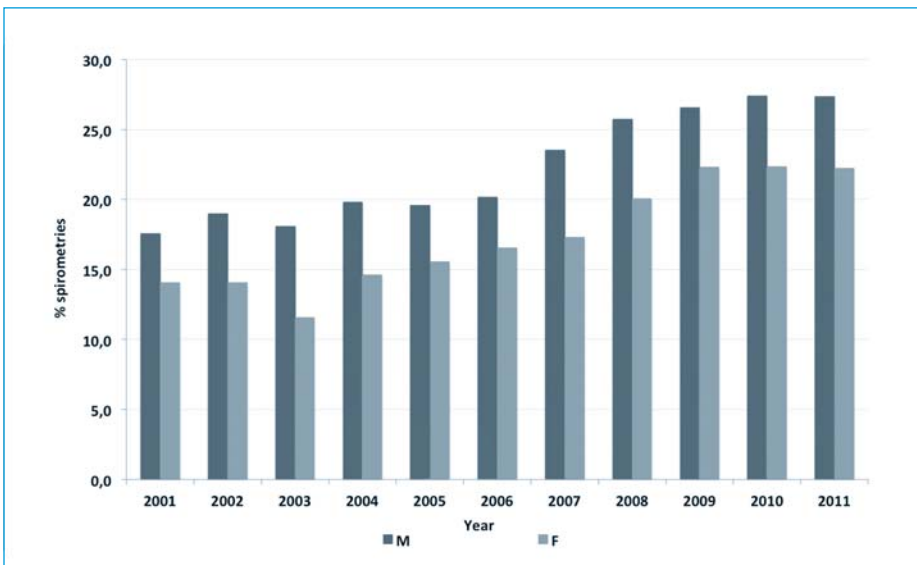
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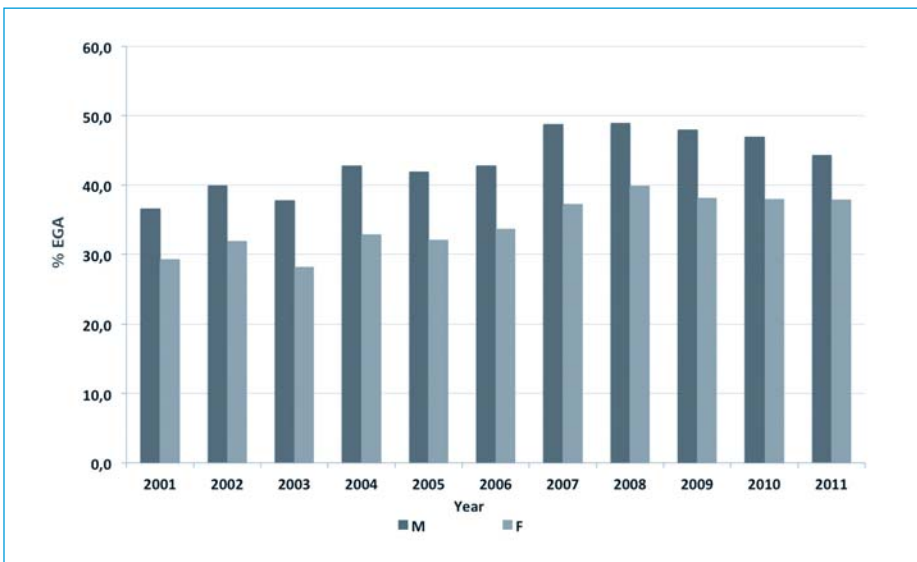
**Figure 5.** Percentage of patients who had a hospitalization in 2009 and repeated it in 2010 or 2011, by sex.

**Table 4.** Percentages of hospital discharges with comorbidities by type of comorbidity and gender. Puglia, 2001-2011.

Comorbidities	% F	% M	% Total
Obesity	7.3	4.0	5.1
Diabetes	19.9	15.4	16.8
Atrial fibrillation	9.7	7.0	7.9
Hypertension	17.8	16.3	16.8
Heart failure	2.9	2.4	2.5
Anxiety disorders	4.2	2.4	3.0



**Figure 6.** Percentage of SDO (patient discharge database) reporting for spirometry, by sex. Puglia, 2001-2011.



**Figure 7.** Percentage of SDO (patient discharge database) reporting for arterial blood gas analysis (EGA), by sex. Puglia, 2001-2011.

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